

DOCKET NO.: UPN-3983
SERIAL NO.: 09/888,860

PATENT
FILED: June 25, 2001

REMARKS

Claims 1-16 are pending in the present application. Claim 8 has been amended. New claim 17 has been added, support for which can be found in, for example, as-filed claim 8. No new matter has been added. Upon entry of the present amendment, claims 1-17 will be pending.

As a preliminary matter, Applicants acknowledge receipt of the "Attachment for PTO-948" outlining changes for prosecution of applications containing drawings. Formal drawings have been filed on date even herewith under separate cover to the Draftsperson.

I. The Claims Are Clear And Definite

Claim 8 is rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. The Office Action asserts that the phrase "such as" renders claim 8 indefinite. Applicants have amended claim 8 to delete "such as" and place the particular viral enhancers in new dependent claim 17. Claim 8 has not been narrowed. Thus, claim 8 is clear and definite. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, second paragraph be withdrawn.

II. The Claimed Invention Is Novel

A. The Stratagene Catalog

Claims 1-8 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by the 1992 Stratagene Catalog (a copy of the 1994 Stratagene Catalog was provided). Applicants traverse the rejection and respectfully request reconsideration because the Stratagene Catalog does not teach every feature recited in claims 1-8.

The Office Action asserts that the pBK-CMV vector contains a T7 promoter in the opposite orientation compared to other promoters such as lac promoter, bla promoter, a T3 promoter and a SV40 promoter. The Stratagene catalog, however, asserts that the T7 promoter is used for *in vitro* transcription, not for *in vivo* expression. Rather, it is either the *lacZ* promoter or CMV immediate early promoter that drives expression in prokaryotes and eukaryotes, respectively (see, description

of prokaryotic and eukaryotic expression on page 19 of the catalog). Thus, there is no promoter in the pBK-CMV vector shown in the Stratagene Catalog that expresses an antisense molecule due to being in reverse orientation compared to the promoter responsible for protein expression. That is, there is no promoter depicted in the pBK-CMV vector that is in reverse orientation compared to either the *lacZ* or CMV promoter that is used for *in vivo* expression. In addition, the pBK-CMV vector depicted does not contain an enhancer (as recited in claims 3 and 8), or a lac promoter, which as the second promoter, is in reverse orientation compared to the first promoter (as recited in claim 5).

The Office Action also asserts that the pPbac vector contains two promoters, P10 and POLH, which are in reverse orientation. Although these promoters are in opposite orientation, it is the POLH promoter that drives expression of the gene to be expressed, which is inserted into the *SmaI/BamHI* sites of the vector (see description of the vector described at page 45). The P10 promoter, however, is not positioned to produce an antisense molecule directed to the gene that is inserted into the vector. In addition, the pPbac vector depicted does not contain an enhancer (as recited in claims 3 and 8), or a lac promoter, which as the second promoter, is in reverse orientation compared to the first promoter (as recited in claim 5).

Thus, the Stratgene Catalog does not teach every feature recited in claims 1-8. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §102 be withdrawn.

B. The Invitrogen Catalog

Claims 1-4, 6, 7, 13 and 15 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by the 1994 Invitrogen Catalog. Applicants traverse the rejection and respectfully request reconsideration because the Invitrogen Catalog does not teach every feature recited in claims 1-4, 6, 7, 13 and 15.

The Office Action asserts that the p2Bac vector contains a first promoter, Ppol, and a second promoter, p10, in opposite orientations. Although these promoters are in opposite orientation, as asserted in the Invitrogen catalog, these promoters permit simultaneous expression of two recombinant proteins from the same construct. The p2Bac vector is not constructed so as to comprise

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a second promoter that produces an antisense molecule directed to a gene when the gene is inserted into the polylinker and whose expression is driven by the first promoter. In addition, the p2Bac vector depicted does not contain a SV40 polyadenylation signal (as recited in claim 6) or mammalian cells comprising a vector of claim 1 (as recited in claim 15).

Thus, the Invitrogen Catalog does not teach every feature recited in claims 1-4, 6, 7, 13 and 15. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §102 be withdrawn.

C. The Matthey Reference

Claims 1, 2, 5, 7, 9, 10 and 12-14 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Matthey *et al.*, *Gene*, **1999**, 229, 145-153 (hereinafter, the "Matthey reference"). Applicants traverse the rejection and respectfully request reconsideration because the Matthey reference does not teach every feature recited in claims 1, 2, 5, 7, 9, 10 and 12-14.

The Office Action asserts that the pBMO.5 vector comprises a pBR322 and fl origin of replication, a T7 lac promoter, a polylinker, and a kanamycin selectable marker. The Office Action asserts that a truncated *Pseudomonas* exotoxin gene (ETA') was cloned into the polylinker downstream of the T7 lac promoter. The Office Action also asserts that the kanamycin gene is transcribed in the opposite orientation of ETA' and that the promoter for kanamycin is inherent. Even if all these observations are correct, and Applicants make no such confirmation, none of the vectors depicted in Figure 1 of the Matthey reference anticipate any of the claims of the present application. For example, none of the vectors of the Matthey reference comprise a promoter that drives expression of a gene (i.e., Applicants' first promoter) and a second promoter that drives production of an antisense molecule directed to that gene when the gene is inserted into the polylinker (i.e., Applicants' second promoter). There is no evidence of record that unequivocally states that the promoter responsible for kanamycin resistance also drives the production of an antisense molecule directed to the gene inserted into the polylinker. Indeed, as stated in the Office Action, a poly(A) signal is located in the 3' end of the kanamycin coding sequence.

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Thus, the Matthey reference does not teach every feature recited in claims 1, 2, 5, 7, 9, 10 and 12-14. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §102 be withdrawn.

III. The Claimed Invention Is Not Obvious

Claims 11 and 16 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the combination of the Invitrogen Catalog or Stratagene Catalog with Bukrinsky *et al.*, *Gene*, **1988**, 70, 415-417 (hereinafter, the "Bukrinsky reference"). The Office Action mistakenly asserts that it would have been *prima facie* obvious for one skilled in the art to have inserted the HIV *env* gene into p2Bac or pBK-CMV. Applicants traverse the rejection and respectfully request reconsideration because there is no motivation to combine the cited references and, even if combined, the claimed invention would not be produced.

The deficiencies of both the Stratagene and Invitrogen Catalogs are incorporated herein by reference for the sake of brevity. The Bukrinsky reference does not cure any of these deficiencies.

There is no motivation to combine the contents of either of the Stratagene or Invitrogen Catalogs with the Bukrinsky reference. One skilled in the art designing a vector for expressing the HIV-1 *env* gene having the features recited in Applicants' claim 1 would not be motivated to use any of the vectors depicted in the pages of the catalogs provided by the examiner. Indeed, none of the vectors depicted in the pages provided by the examiner contain the features recited in claim 1. One skilled in the art would recognize that such vectors do not produce antisense molecules directed to the toxic gene when the toxic gene is inserted into the polylinker of the vector. Thus, one skilled in the art would not even seek to make such a combination. However, if one skilled in the art were to attempt to combine the teachings of the cited references, the vector recited in Applicants' claim 1 would not be produced for the reasons discussed above.

Thus, the claimed invention is not obvious in view of the combination of cited references. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §103(a) be withdrawn.

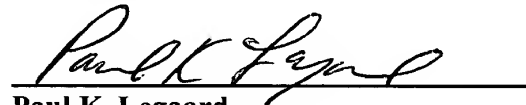
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IV. Conclusion

In view of the foregoing, Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The examiner is invited to contact Applicants' undersigned representative at (215) 665-6914 if there are any questions regarding Applicants' claimed invention. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

Respectfully submitted,



Paul K. Legaard
Registration No. 38,534

Date: 16 December 2002

COZEN O'CONNOR
1900 Market Street
Philadelphia, PA 19103-3508
Telephone: (215) 665-6914
Facsimile: (215) 701-2141



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

New claim 17 has been added.

Claim 8 has been amended as follows:

8. (Amended) The vector of claim 3 wherein said enhancer is selected from the group consisting of rous sarcoma virus enhancer, human actin enhancer, human myosin enhancer, human hemoglobin enhancer, human muscle creatine enhancer, viral enhancers [such as those from cytomegalovirus and Epstein-Barr virus], immunoglobulin enhancers, class II enhancers, and enhancers active in dendritic cells and macrophages.